
2014 Cardiovascular Risks Standing Review Panel

*Evidence Review for:
The Risk of Orthostatic Intolerance During Re-Exposure to Gravity*

Final Report

I. Executive Summary and Overall Evaluation

The 2014 Cardiovascular Risks Standing Review Panel (from here on referred to as the SRP) met for a site visit in Houston, TX on December 17-18, 2014. The SRP reviewed the updated evidence report for The Risk of Orthostatic Intolerance During re-Exposure to Gravity (OI Risk).

The SRP found the 2014 OI Evidence Report to be a well written, comprehensive overview of the OI risk; that clearly documents the key scientific evidence relevant for both mechanistic understanding and countermeasure development. The 2014 OI Evidence Report could be further strengthened by addressing the points discussed below.

II. Review of the Evidence for the Risk of Orthostatic Intolerance during Re-Exposure to Gravity

1. Evaluate the 2014 Orthostatic Intolerance (OI) Evidence Report using the following criteria:

A. Does the 2014 Evidence Report provide sufficient evidence that the Risk is relevant to long-term space missions?

Yes, the SRP found that the 2014 OI Evidence Report provides enough evidence that the OI Risk is relevant to long-duration space missions.

*B. Are the Risk Title and Statement properly stated in the current version of the HRP Integrated Research Plan (IRP)?**

Yes, the SRP considers the Risk Title and Statement properly stated.

C. Is the text of the Risk Context provided in the HRP IRP clear?

Yes, the Risk Context text in the HRP IRP is clear.

D. Does the evidence base make the case for the knowledge-type gaps presented?

Yes, the SRP agrees that the evidence base presented in the 2014 OI Evidence Report makes the case for the knowledge-type gaps presented.

E. Are there any additional knowledge-type gaps that should be considered for this specific Risk?

The SRP recommends additional knowledge-type gaps that should be discussed in the 2014 OI Evidence Report, including:

- 1) OI on return from microgravity to 1G is common, more severe with longer exposure to microgravity, and has potential adverse consequences. Many years of investigation of both return to Earth and head-down bed rest studies have defined the epidemiology, mechanisms and countermeasures for OI. When considering the data concerning the incidence of OI following short- and long-duration missions, the SRP noted that individuals who were unable to complete orthostatic maneuvers following re-exposure to gravity were excluded from the analyses. It would be helpful to see data showing whether they were excluded for technical reasons or if they had such severe OI that they could not take part in a stand or tilt test. In addition, it would be helpful to know the atmospheric carbon dioxide (CO₂) at landing, since a sudden decrease in CO₂ can decrease cerebral blood flow (Loveman et al. Diving Hyperb Med. 2014¹).
- 2) Studies in the past year highlight a new compression garment which shows impressive efficacy preventing OI when combined with salt and water loading. Data was not presented by the cardiovascular discipline lead, Dr. Stenger, concerning the potential for overheating in astronauts donning and wearing the garment, but it will retain heat much less than inflatable garments and is less bulky and lighter. Members of the SRP were impressed with the efficacy of the new compression garment and think that some further studies that outline its performance in simulated 3/8 Mars gravity and in circumstances that model landing emergencies could further define its practical application to spaceflight.
- 3) Studies on a new compression garment completed in the last year have demonstrated impressive efficacy on return from the International Space Station (ISS). The studies have been carried out on astronauts who have ingested about 10 grams of salt in space with at least a liter of water. They then received 1 liter of normal saline prior to testing. Compression garments prevent pooling of blood in the legs and abdomen and return blood toward the heart. Efficacy of the garments depends on the blood volume available for compression. The effect of this new garment on subjects who do not have an infusion of saline would be helpful, since saline infusion would not be available in an emergency egress.
- 4) The new compression garment may be so effective that it provides excess compression for 3/8 gravity found on Mars. Studies on the effect of the new garment on fluid distribution, blood pressure and heart rate in response to a partial tilt on a tilt table could help determine if less compression is appropriate for lower gravitational forces. It is likely that a garment with less compression would be appropriate for landing in the lesser gravitational force of Mars.

F. Does the Evidence Report address relevant interactions between this Risk and others in the HRP IRP?

The interactions between the OI risk and other risks in the HRP IRP are not specifically addressed in the 2014 OI Evidence Report. A brief synopsis of these interactions would be helpful to identify areas where interdisciplinary studies are required.

During the 2014 meeting, Dr. Stenger pointed out a number of existing interactions with the nutrition lab, the exercise physiology lab, the neurosciences lab, and the visual impairment and intracranial pressure (VIIP) team. Perhaps a section should be added to the Evidence Report to discuss these interdisciplinary efforts.

G. Are the qualifications of the author(s) appropriate for identifying the evidence base necessary to characterize the given Risk?

Yes, the SRP thinks the team is very knowledgeable, has the appropriate expertise and backgrounds to make assessments.

H. Is there information from other HRP disciplines that need to be included in the 2014 Evidence Report?

As fluid and salt loading are countermeasures for OI, information from the nutrition group would seem to be appropriate.

I. Is the breadth of the cited literature sufficient?

Yes, the authors have cited a comprehensive breadth of literature.

J. What is the overall quality and readability of the 2014 Evidence Report?

The 2014 OI Evidence Report is a comprehensive document that provides an excellent overview of relevant scientific findings related to the risk of post-flight OI and the countermeasures that have been developed and tested to ameliorate OI. In general, it is a well written, scholarly document. The color-coding in Figure 16 of the 2014 OI Evidence Report appears to be incorrect and improvements could be made to a few of the figures containing low-magnification, low-resolution images (Figures. 23, 24, 25).

III. References

- 1) Loveman GA, Seddon FM, Thacker JC, White MG, Jurd KM. Physiological effects of rapid reduction in carbon dioxide partial pressure in submarine tower escape. *Diving Hyperb Med.* 2014 Jun;44(2):86-90.

IV. 2014 Cardiovascular Risks SRP Evidence Review: Statement of Task for the Risk of Orthostatic Intolerance During Re-Exposure to Gravity

In 2008, the Institute of Medicine (IOM) reviewed NASA's Human Research Program (HRP) Evidence Books that describe the Risks that were identified in NASA's Human Research Program Requirements Document (PRD). The 2014 Evidence Report for the Risk of Orthostatic Intolerance During Re-Exposure to Gravity (OI) has not been reviewed since the last IOM review and there have been significant changes to the evidence base for the Risk.

The 2014 Cardiovascular Risks Standing Review Panel (SRP) is chartered by the Human Research Program (HRP) Chief Scientist to review the Evidence Report for the OI Risk. The 2014 Cardiovascular Risks SRP will evaluate the Evidence Report and generate a final report of your analyses of the evidence base, including any recommendations on how to improve the current Evidence Report, and submit it to the HRP Chief Scientist. Your report will also be made available on the Human Research Roadmap (HRR) website.

The 2014 Cardiovascular Risks SRP is charged to:

1. Evaluate the 2014 OI Evidence Report based on each of the following criteria:
 - A. Does the 2014 Evidence Report provide sufficient evidence that the Risk is relevant to long-term space missions?
 - B. Are the Risk Title and Statement properly stated in the current version of the HRP Integrated Research Plan (IRP)?*
 - C. Is the text of the Risk Context provided in the HRP IRP clear?*
 - D. Does the evidence base make the case for the knowledge-type gaps presented?
 - E. Are there any additional knowledge-type gaps that should be considered for this specific Risk?
 - F. Does the Evidence Report address relevant interactions between this Risk and others in the HRP IRP?
 - G. Are the qualifications of the author(s) appropriate for identifying the evidence base necessary to characterize the given Risk?
 - H. Is there information from other HRP disciplines that need to be included in the 2014 Evidence Report?
 - I. Is the breadth of the cited literature sufficient?
 - J. What is the overall quality and readability of the 2014 Evidence Report?
2. Provide comments on any important issues that are not covered by the criteria in #1 above.

* Please be aware that any suggested changes to the Risk Title, Statement, and Risk Context by the SRP may need to be approved by the Human Systems Risk Board (HSRB). The HSRB has the overall responsibility to implement and maintain a consistent, integrated process for assessing, documenting, and tracking all risks to the human system associated with spaceflight activities (both in flight and post flight).

Additional information regarding this review:

1. Attend a meeting in Houston, TX on December 17 - 18, 2014 to discuss the Evidence Report with the Human Health Countermeasures (HHC) Element. At this meeting, prepare a draft report for each risk that addresses each of the evaluation criteria listed in the panel charge (A-J) including any recommendations on how to improve the Evidence Report. Debrief the HRP Chief Scientist and a representative from the HHC Element on the salient points that will be included in the final report and specifically the items in the panel charge.
2. Prepare a draft final report for each risk (within one month of the site visit debrief) that contains a detailed evaluation of the Evidence Report specifically addressing items #1 and #2 of the SRP charge. The draft final report will be sent to the HRP Chief Scientist and he will forward it to the appropriate Element for their review. The HHC Element and the HRP Chief Scientist will review the draft final report and identify any misunderstandings or errors of fact and then provide official feedback to the SRP within two weeks of receipt of the draft report. If any misunderstandings or errors of fact are identified, the SRP will be requested to address them and finalize the 2014 SRP Final Report as quickly as possible. The 2014 SRP Final Report will be submitted to the HRP Chief Scientist and copies will be provided to the HHC Element that sponsors the cardiovascular discipline and also made available to the other HRP Elements. The 2014 SRP Final Report will be made available on the HRR website (<http://humanresearchroadmap.nasa.gov/>).

To clarify, the Risk Statement and Risk Context are defined as follows:

Risk Statement:

“Given the CONDITION, there is a possibility that a CONSEQUENCE will occur”.

Condition: a single phrase briefly describing current key circumstances, situations, etc. that are causing concern, doubt, anxiety, or uncertainty – something that keeps you up at night.

Consequence: a single phrase or sentence that describes the key, negative outcome(s) of the current conditions.

Notes:

The condition-consequence format provides a more complete picture of the Risk, which is critical during mitigation planning. The condition component focuses on what is currently causing concern. This is something that is true or widely perceived to be true. This component provides information that is useful when determining how to mitigate a Risk.

The consequence component focuses on the intermediate and long-term impact of the risk. Understanding the depth and breadth of the impact is useful in determining how much time, resources, and effort should be allocated to the mitigation effort.

A well-formed Risk Statement usually has only one condition, and has one or more consequences.

Risk Context:

Purpose: provide enough additional information about the Risk to ensure that the original intent of the Risk can be understood by other personnel, particularly after time has passed.

Description: capture additional information regarding the circumstances, events, and interrelationships not described in the Risk Statement.

An effective context captures the what, when, where, how, and why of the Risk by describing the circumstances, contributing factors, and related issues (background and additional information that are NOT in the Risk Statement).

V. 2014 Cardiovascular Risks SRP Roster

Panel Chair:

Michael Ziegler, M.D.

UCSD Medical Center

200 West Arbor Drive

San Diego, CA 92103

Ph: 619-543-2885

Email: mziegler@ucsd.edu

Panel Members:

Jason Carter, Ph.D.

Michigan Technological University

Department of Kinesiology and Integrative Physiology

1400 Townsend Drive

Houghton, MI 49931

Ph: 906-487-2715

Email: jcarter@mtu.edu

Victoria Claydon, Ph.D.

Simon Fraser University

Department of Biomedical Physiology and Kinesiology

8888 University Drive

Burnaby, British Columbia, V5A 1S6

Canada

Ph: 778-782-8513

Email: victoria_claydon@sfsu.ca

David Krummen, M.D.

VA San Diego Medical Center/UCSD

Sulpizio Cardiovascular Center

14168 Half Moon Bay Drive

Del Mar, CA 92014

Ph: 858-922-9275

Email: dkrummen@ucsd.edu

Gail Thomas, Ph.D.

Penn State Heart and Vascular Institute

Penn State College of Medicine

500 University Drive

Hershey, PA 17033

Ph: 717-531-0003, ext. 287087#

Email: gthomas4@hmc.psu.edu